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Activated Iodosylbenzene Monomer as an Ozone Equivalent: Oxidative Cleavage of Carbon−Carbon Double Bonds in the Presence of Water

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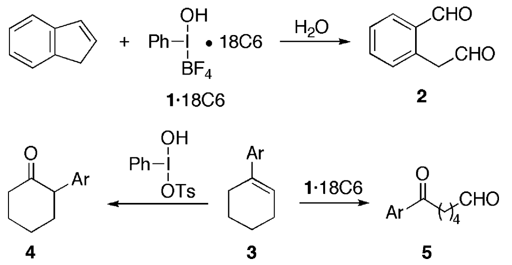
Hypervalent aryl-λ^3-iodanes with two heteroatom ligands on iodine(III) have emerged as reagents of choice for oxidations of a broad range of functionalities, mostly because of their environmentally friendly nature and high selectivity.[1] They undergo vicinal difunctionalizations of olefins under mild conditions, and a wide range of functional groups (OAc, $OClO_3$, OTs, OMs, OTf, $OCOCF_3$, SPh, SCN, SePh, N_3, F, Cl, etc.) are introduced mostly with high 1,2-syn stereoselectivity. The accepted mechanism involves an initial electrophilic anti addition of λ^3-iodanes to a double bond and a subsequent nucleophilic displacement of the aryl-λ^3-iodanyl group with inversion of configuration at the carbon atom.[1] To our surprise, however, there have been no reports in the literature on direct vicinal dihydroxylations of double bonds using aryl-λ^3-iodanes.[2]

Hypervalent λ^3-iodane such as (diacetoxyiodo)benzene or iodine triacetate undergoes smooth oxidative cleavage of the glycol C−C bond probably via the intervention of cyclic dialkoxy-λ^3-iodanes, yielding carbonyl compounds.[3,4] A large and rigidly held distance between the two oxygen atoms is shown to dramatically decrease the rate of glycol fission.[3b] It occurred to us that the development of direct syn *vic*-dihydroxylation of olefins using aryl-λ^3-iodanes, combined with the oxidative glycol fission, will make it possible to cleave the carbon−carbon double bonds in one-pot.

Oxidative cleavage of a carbon−carbon double bond to carbonyl compounds is an essential operation in organic synthesis.[5] Ozonolysis is generally accepted as the standard method for this direct transformation;[6] however, its utility is often limited by safety concerns.[7] Use of high-valent oxometals such as RuO_4, OsO_4, and $MeReO_3$ in combination with a number of oxygen donors ($NaIO_4$, Oxone, or Jones reagent) as stoichiometric oxidants is suitable for the oxidative catalytic cleavage of olefins,[8] but they are expensive and/or toxic. Therefore, the development of a safe and environmentally friendly procedure for the cleavage of carbon−carbon double bonds is highly desirable. We report herein for the first time that protonated iodosylbenzene monomers directly undergo the oxidative cleavage of olefins at room temperature in aqueous media.

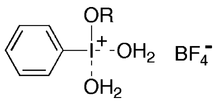
We recently reported a synthesis of protonated iodosylbenzene monomer•18-crown-6 complex **1**•18C6 as stable crystals, which serves as an efficient oxidant for a variety of functional groups such as olefins, alkynes, enones, silyl enol ethers, sulfides, and phenols under mild conditions, especially in water as a solvent.[9] Exposure of indene to the hydroxy-λ^3-iodane complex **1**•18C6 (2.2 equiv) in water resulted in a smooth cleavage of the double bond within 3 h at room temperature: a labile dialdehyde **2** was selectively produced in 87% yield (^{1}H NMR) and the corresponding diol (76%) was isolated after reduction with $NaBH_4$ in methanol (Scheme 1). This is the first example of oxidative cleavage of simple olefins with aryl-λ^3-iodanes. Very interestingly, in marked contrast to the Koser reagent PhI(OH)OTs that affords a rearranged α-phenyl ketone **4a** (84%) by the reaction with 1-phenylcyclohexene (**3a**) in 95% methanol,[10] the complex **1**•18C6 undergoes oxidative cleavage of the double bond in water yielding keto aldehyde **5a** selectively, albeit in a moderate yield (23%), with a large amount of the recovered olefin **3a** (54%). 18C6 tightly coordinates to the iodine center in $PhI(OH)BF_4$ **1** as a tridentate ligand and hence enhances its thermal stability,[9a] which is responsible, at least in part, for the moderate reactivity of the complex **1**•18C6.

Scheme 1



Ar: **a** (Ph), **b** (p-MeC_6H_4), **c** (p-ClC_6H_4), **d** (p-$CF_3C_6H_4$).

After extensive studies on reaction conditions, we found efficient general methods for the oxidative cleavage of olefins, which involve the in situ generation of λ^3-iodane **1** from iodosylbenzene without adding 18C6 in the presence of water: method A, PhIO (2.2 equiv)/48% aqueous HBF_4 (6 equiv)/CH_2Cl_2−H_2O 9:1/room temperature; method B, PhIO (2.2 equiv)/48% aqueous HBF_4 (2.2 equiv)/CH_2Cl_2-hexafluoroisopropanol (HFIP)-H_2O 9:3:1/room temperature. Hydroxy-λ^3-iodane **1** is labile in dichloromethane solution and decomposes at room temperature within a few minutes to give a black tar;[11] however, we found that iodane **1** is a stable species with a half-life time of several days at 23 °C when generated in water (Supporting Information, Figure S1). Tetracoordinated square-planar hydroxy-λ^3-iodane **6a**, with two water molecules being coordinated to the iodine center,[9b,12] will probably exist as an activated iodosylbenzene monomer under our conditions.[13]



6a: R = H
6b: R = $CH(CF_3)_2$

Cleavage efficiency of the olefin **3a** was greatly improved under these conditions and both methods A and B afforded good yields (75−80%) of keto aldehyde **5a** (Table 1, entries 7 and 8). In the reaction of an electron rich olefin **3b**, method B afforded a large amount of the rearranged ketone **4b** (38%), while method A showed higher selectivity for double bond cleavage over 1,2-aryl migration (entries 9 and 10). Use of HFIP (method B) probably slows down the rate of formation of intermediate *vic*-diols via S_N2 displacement of phenyl-λ^3-iodanyl group with water, because of the decreased nucleophilicity of water through hydrogen bonding with acidic HFIP ($pK_a = 9.3$),[14,15] which in turn resulted in the formation of substantial amounts of the migration product **4b**. On the other hand, the attempted cleavage of a less reactive olefin **3d** with an electron-withdrawing p-CF_3 group using method A was found to be fruitless, while use of HFIP afforded a good yield of **5d** (71%) (entries 13 and 14), which indicates that method B is a favorable choice for the cleavage of less reactive olefins.[16]

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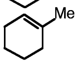
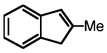
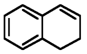
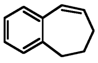
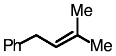
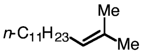
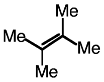
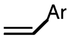
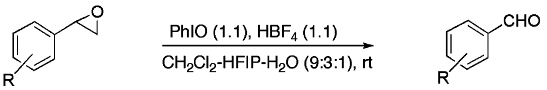
Table 1. Oxidative Cleavage of Olefins with Iodosylbenzene

entry	olefin	method[a]	time h	yield (%)[b]
1		B	1	79 (50)
2		B	1.5	80 (41)
3		A	0.5	53
4		A	2	76 (72)
5		A	3	(57)
6		B	1.5	58 (44)
7	**3a**	A	2	75 (82)
8	**3a**	B	2	80 (77)
9	**3b**	A	1	66 (64)[c]
10	**3b**	B	1	56 (57)[c]
11	**3c**	A	5	61 (56)
12	**3c**	B	2	83 (84)
13	**3d**	A	8	13[d]
14	**3d**	B	4	71 (66)
15		B	2	57 (57)
16		B	2	54 (55)
17		A	2	(72)[e]
				
18	Ar = Ph	B	1	4 (5)[f]
19	m-$CF_3C_6H_4$	B	8	57 (54)[f]
20	p-$CF_3C_6H_4$	B	8	67 (53)[f]
21	p-$MeO_2CC_6H_4$	B	4	58 (54)[f]
22	m-$NO_2C_6H_4$	B	72	61 (56)[f]

[a] See text. [b] Yields of carbonyl compounds were determined by ^1H NMR. Parentheses are isolated yields of alcohols (or their derivatives), after reduction with $NaBH_4$ in MeOH. [c] Yields of byproduct **4b**: 17% (entry 9) and 38% (entry 10). [d] Olefin **3d** (46%) was recovered. [e] Isolated as 2,4-(dinitrophenyl)hydrazone. [f] Yields of phenylacetaldehydes: 85%, 24%, 21%, 32%, and 8% for entries 18−22.

Cyclic (cyclopentenes, cyclohexenes, etc., entries 1−6) and acyclic (entries 15−17) olefins are cleaved smoothly under our conditions. With styrene, however, 1,2-phenyl migration yielding phenylacetaldehyde was proved to be a principal reaction pathway (entry 18), as reported by Moriarty and Koser.[10,17] In contrast, electron-deficient styrenes with CF_3, CO_2Me, and NO_2 groups primarily undergo the oxidative cleavage yielding substituted benzaldehydes in good yields, being accompanied by formation of the rearranged phenylacetaldehydes (entries 19−22). Ratios of the oxidative cleavage to rearrangement products depend on the electronic nature of the aryl groups, and a linear Hammett relationship ($\rho = 3.1$) for the substituent effects with $r = 0.98$ was found between $\log(k_{ArCHO}/k_{ArCH2CHO})$ and σ values (Figure S2).

Scheme 2



R (reaction time h, yield): H (1, 89%), p-Me (2, 57%)), p-Cl (5, 75%), m-CF_3 (6, 69%), p-CF_3 (8, 70%), p-MeO_2C (5.5, 64%), m-NO_2 (42, 88%).

The cleavage of m-nitrostyrene is very slow and requires a prolonged reaction time (3 days, entry 22). Interestingly, formation of a considerable amount (34%) of the corresponding epoxide together with m-$NO_2C_6H_4CHO$ (39%) was detected when the reaction was quenched after 25 h. These results appear to indicate the intermediacy of epoxides on the way to the formation of the cleaved products from styrenes at least in part. Iodosylbenzene and its derivatives transfer the oxygen atom to highly electron-deficient olefins, affording epoxides.[18] In fact, we found that a variety of aryloxiranes undergo an oxidative cleavage of the epoxide rings under the conditions similar to method B and aromatic aldehydes were obtained in good yields (Scheme 2).[19,20]

In summary, we have developed an efficient method for the oxidative cleavage of carbon−carbon double bonds as a safety alternative to ozonolysis, by using a combination of iodosylbenzene and HBF_4 in the presence of water.

Supporting Information Available: Experimental details and Figures S1−S4. This material is available free of charge via the Internet at http://pubs.acs.org.

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